REMARKS

Upon entry of the foregoing amendment, claims 10–32 are pending for the Examiner's consideration with claims 10, 25 and 26 being the independent claims. Claims 2 and 5-9 stand rejected. Claims 2 and 5–9 are canceled for the purpose of expediting prosecution. Claims 10–32 are new claims. Applicants respectfully submit that the present amendment introduces no new matter. In this regard, the Examiner is referred to the application as originally filed at, for example, page 9, line 20 to page 12, line 24; page 22, line 27 to page 24, line 26 and original claims 1-5.

Applicants amend the specification to expedite prosecution by inserting "SEQ ID NO: 7" after "HPTPbeta catalytic domain" in the Brief Description of the Drawings and Tables section. It is believed that these changes to the specification do no involve the introduction of new matter. Accordingly, entry of these changes is respectfully requested.

Compliance with 37 C.F.R. §§ 1.821–1.825

The Examiner maintains the contention that the instant Application does not comply with the sequence requirements of 37 C.F.R. §§ 1.821–1.825. According to the Examiner, "each time in the specification the phrase 'HPTPbeta' appear to refer to a specific amino acid sequence or nucleic acid in the sequence listing, a sequence identification number should follow the phrase (see for example the Figures descriptions . . .)." Office Action, page 2. In Applicants' Reply After 1st Office Action Under 37 C.F.R. § 1.111(b) dated October 12, 2006 (the "previous Reply"), Applicants included an amendment to the specification which added references to SEQ ID NO. 7 in the Brief Description of the Drawings and Table. However, the Examiner alleges that "[t]he atomic coordinates Tables of Figures 7-304 constitute the disclosure of linear amino acid sequences for an amino acid sequence in the sequence listing." *Id.* The Examiner further states: "Thus, either the Tables should have a heading with the sequence identifier or the Figures descriptions contain a sequence identifier. Also, the claims are not in compliance with the sequence rules and the sequence identifier must be inserted each time after the phrase 'HPTPbeta,' wherever it appears." *Id.* (emphasis in original).

Applicants respectfully point out that, contrary to the statement in the Office Action, the Tables set forth in Figures 7–304 do not constitute a "linear amino acid sequence[]." *Id.* Rather, the Tables set forth X, Y and Z coordinates of a three-dimensional peptide structure. An amino acid structure defined in three dimensions is not a "linear" amino acid sequence, which is not defined in three dimensions. However, solely to expedite prosecution, Applicants amend the specification to add SEQ ID NO: 7 after "HPTPbeta catalytic domain" to comply with the Examiner's request that "the Figures descriptions contain a sequence identifier," although Applicants maintain the position that the Figures 7–304 set forth the coordinates of a three-dimensional peptide structure.

The Office Action further contends, as noted above, that "the sequence identifier must be inserted each time after the phrase 'HPTPbeta,' wherever it appears." *Id.* Applicants respectfully point out that, under M.P.E.P. § 2422.03 at 2400-34 (8th ed., rev. no. 5), Applicants are not required to use a sequence identification number after each occurrence of the term 'HPTPbeta.' According to § 2422.03:

> In those instances in which prior art sequences are only referred to in a given application by name and a publication or accession reference, they need not be included as part of the "Sequence Listing," unless an examiner considers the referred-to sequence to be "essential material," per M.P.E.P. § 608.01(p).

Id. The specification of the instant Application indeed discloses a "name and a publication . . . reference" of the HPTPbeta sequence at page 1, line 13. As a courtesy to the Examiner, Applicants include herein a copy of the referenced publication, Krueger *et al.*, "Structural Diversity and Evolution of Human Receptor-Like Protein Tyrosine Phosphatases," *EMBO J.* 9:3241–3252 (1990).[1] Consequently, unless the entire sequence of HPTPbeta is considered to be "essential material," which the Examiner has not heretofore asserted, Applicants are not required to include HPTPbeta as part of the Sequence Listing.[2] Because Applicants are not required to include HPTPbeta as part of the Sequence Listing, Applicants are certainly not required to use a

[1] The Krueger *et al.* article was cited in the Information Disclosure Statement dated December 16, 2003 as Non-Patent Literature Document 7.

[2] Applicants note, however, that the sequence of HPTPbeta is included in the Sequence Listing of the instant Application as SEQ ID NO. 2.

sequence identification number after each occurrence of the term "HPTPbeta" throughout the specification and claims.

Thus, in view of the above remarks, Applicants respectfully submit that the present application complies with 37 C.F.R. §§ 1.821–1.825, and request the Examiner to withdraw the objection.

Rejection Under 35 U.S.C. § 112, ¶ 2

The Examiner maintains the rejection of claims 2 and 5–9 under 35 U.S.C. § 112, ¶ 2, as allegedly being indefinite. The Examiner states that "[t]he clause 'a compound that binds to HPTPbeta *in silico* in claim 2 renders that claim indefinite" and "[t]he phrase '*ex vivo* assay' in claim 5 renders the claim indefinite." *Id.* at 2–3.

Without conceding the propriety of the Examiner's rejection, claims 2 and 5–9 are canceled herein solely to expedite prosecution. New claims 10-29 do not contain the phrase "a compound that binds to HPTPbeta *in silico*" or the phrase "*ex vivo* assay." Therefore, as the rejection of claims 2 and 5 and their dependent claims 6-9 is rendered moot, Applicants respectfully request that the Examiner withdraw the rejection under § 112, ¶ 2.

Rejection Under 35 U.S.C. § 103(a)

The Examiner maintains the rejection of claims 2 and 5–9 under 35 U.S.C. § 103(a) as purportedly rendered obvious by "the commercial availability of computers and various software packages listed in the specification at 10, line 11 through page 11, line 26" in view of Fachinger *et. al.*, "Functional Interaction of Vascular Endothelial-Protein-Tyrosine Phosphatase with the Angiopoietin Receptor Tie-2," *Oncogene*, 18:1189-1198 (1999) (the "Fachinger reference") for the reasons stated in the Office Action mailed April 13, 2006. Office Action, pages 3–4. The Office Action further states:

> The examiner agrees with the applicants that the atomic coordinates for the 3D structure of HPTPbeta catalytic domain are novel. Also, applicants agree that the computers and their software are known. So the difference between the prior, [sic] art which includes motivation to one of ordinary skill in the art to

> identify modulator of HPTPbeta activity, are the atomic coordinates in Figures 7-304. As indicated . . . the atomic coordinates are non-functional descriptive material, which cannot render non-obvious an invention that has otherwise been obvious. See *In re Gulak*, 703 F.2d 1381, 1385 (Fed. Cir. 1983).

Office Action, page 4.

Applicants respectfully disagree. Applicants respectfully point out that Applicants did not, in the previous Reply, and still do not, "agree that the computers and their software are known." *Id.* While Applicants' previous Reply states "the fact that the skilled person may employ previously available software in Applicants [sic] method does not render the method obvious," it is unclear from the Office Action statement to which "computers and their software" the Office Action is now referring. To the extent that Applicants' invention, which relates, in part, to computer-implemented methods, covers such "computers and their software," Applicants maintain that such computers and their software were *not* known in the art prior to Applicants' invention.

Moreover, the Office Action cites *In re Gulak*, 703 F.2d 1381, 1385 (Fed. Cir. 1983) after the statement that "the atomic coordinates are non-functional descriptive material, which cannot render non-obvious an invention that has otherwise been obvious." *Id.* However, the holding in *Gulak* in fact demonstrates that Applicants' claimed invention is non-obvious. In *Gulak* the Court reversed the decision of the Board of Patent Appeals and Interferences and held that claims directed to printed matter on a substrate band were non-obvious despite the fact that the printed matter was in the prior art and, by itself, unpatentable. The Court in Gulak explained:

> The fact that the printed matter by itself is not patentable subject matter, because non-statutory, is no reason for ignoring it when the claim is directed to a combination.
>
> . . . .
>
> [T]he critical question is whether there exists any new and unobvious *functional relationship* between the printed matter and the substrate.

Gulak at 1386 (quoting *In re Miller*, 418 F.2d 1392 (C.C.P.A. 1969)) (emphasis added). In its obviousness analysis, rather than addressing the functionality of the relationship involving the recited atomic coordinates, the Office Action focuses only on the atomic coordinates themselves

and merely contends that "the atomic coordinates are non-functional." Office Action, page 4. Applicants maintain the position that claims 2 and 5–9 are non-obvious, as these claims are directed to more than atomic coordinates and in fact encompass a non-obvious functional relationship involving at least the recited atomic coordinates and the identification of a drug candidate for the treatment of an angiogenesis mediated disorder.

Without conceding the propriety of the rejection and solely to expedite prosecution, claims 2 and 5–9 are canceled, and the rejection of these claims is moot. Applicants respectfully assert that the claimed invention is novel and non-obvious, as neither the cited references nor any other reference, whether alone or in combination, discloses all of the features of Applicant's invention set forth in new claims 10–32.

With regard to new claim 10, no aspect of "the commercial availability of computers and various software packages listed," the Fachinger reference or any other reference, considered alone or in combination, discloses, for example, a computer-implemented method involving determining a three-dimensional structure of all or a portion of a crystalline form of HPTPbeta catalytic domain from the recited X, Y and Z atomic structure coordinates of an HPTPbeta catalytic domain, and identifying drug candidate compounds from compounds that bind or modulate HPTPbeta as compounds useful for the treatment of an angiogenesis mediated disorder. The cited documents cannot disclose or suggest this claimed subject matter because, as the Examiner recognizes, the atomic coordinates of HPTPbeta are novel. *See* Office Action, page 4. Even in light of knowledge imparted by the "computers and various software packages listed," the Fachinger reference and any other reference, because the coordinates of Applicants' invention were not known or suggested to one of skill in the art, the skilled person could not: (i) image a three-dimensional structure of an HPTPbeta catalytic domain; (ii) position candidate compounds at an area of the imaged three-dimensional structure; and (iii) identify candidate compounds that bind or modulate HPTPbeta as drug candidate compounds as required by claim 10. Nothing in any of the references teaches or suggests to the skilled person what the unique three-dimensional coordinates of HPTPbeta are. Hence, the combination of the features recited in claim 10, which encompasses these coordinates, is not rendered obvious by the cited documents.

Similarly, regarding new claims 25 and 26, no disclosure in "the commercial availability of computers and various software packages listed," the Fachinger reference or any other reference, whether taken alone or in combination, discloses, for example, imaging through the use of computer modeling of the recited X, Y and Z atomic structure coordinates, a crystalline form of an HPTP beta catalytic domain using unit cell dimensions of approximately a=39 Å, b=71Å, c=120 Å, α=90°, β=90°, γ=90° in the space group $P2_12_12_1$ or a=62 Å, b=72 Å, c=70 Å, α=90°, β=93°, γ=90° in the space group $P2_1$, and analyzing the ability of a drug candidate compound to bind or modulate HPTPbeta in an *in vivo* or *in vitro* assay. Because the coordinates of Applicants' invention were not known or suggested to one of skill in the art, even in view of "computers and various software packages listed," the Fachinger reference and any other reference, the skilled person could not: (i) image, through the use of computer modeling of X, Y and Z atomic structure coordinates, an HPTPbeta catalytic domain; (ii) position a drug candidate compound at an area of an imaged HPTPbeta catalytic domain; and (iii) analyze the ability of the drug candidate to bind or modulate HPTPbeta, as required by claims 25 and 26. Nothing in any of the references teaches or suggests to one of skill in the art the three-dimensional coordinates of HPTPbeta. Furthermore, without the three-dimensional coordinates of HPTPbeta, one of skill would not know the unit cell dimensions of an HPTPbeta catalytic domain required of claim 25 of approximately a=39 Å, b=71Å, c=120 Å, α=90°, β=90°, γ=90° in the space group $P2_12_12_1$, or the unit cell dimensions of an HPTPbeta catalytic domain required of claim 26 of approximately a=62 Å, b=72 Å, c=70 Å, α=90°, β=93°, γ=90° in the space group $P2_1$. As the combination of the features in each of claims 25 and 26 encompasses these unique three-dimensional coordinates and unit cell dimensions of an HPTPbeta catalytic domain, claims 25 and 26 are not rendered obvious by the cited documents.

Indeed, at least one aspect of the non-obviousness of Applicants' invention can be analogized to the non-obviousness of the claims at issue in *Gulak*. As discussed above, in *Gulak*, the claims were directed to printed matter on a substrate band. *Gulak*, 703 F.2d at 1383. The Board did not give the printed matter patentable weight. *Id.* at 1384. In reversing the Board's decision, the Court recognized ways in which the printed matter was related to the substrate band. *Id.* at 1386. The Court therefore concluded that the digits in the printed matter "exploit the . . . nature of the band" and found a functional relationship between the printed matter and the band. *Id.* at 1387. Determining that the functional relationship was different

from the relationship found in the prior art reference, the Court held that the appellant's invention was non-obvious. *Id.*

Similarly, Applicants' inventive methods, involve, in key part, a non-obvious functional relationship between X, Y and Z coordinates and a drug candidate compound. Applicants' claimed methods involve positioning a candidate compound at an area of an imaged HPTPbeta domain. This act of positioning a compound has a crucial functional and structural relationship with the coordinates. The coordinates define the three-dimensional structure of HPTPbeta in relation to space and in relation to itself. Thus, the coordinates are responsible for the special nature of the three-dimensional HPTPbeta structure. The positioning of the compound occurs relative to the three-dimensional HPTPbeta structure. One cannot position a compound in some orientation to an area of HPTPbeta without accessing this special nature of the three-dimensional structure. In this manner, the positioning of the compound is critically related to the unique three-dimensional coordinates of HPTPbeta. As in *Gulak*, the claimed feature "exploit[s]" the nature of another feature to which it is functionally related. *Id.* In Applicants' inventive methods, the use of X, Y and Z coordinates of HPTPbeta "exploits" the particular nature of a drug candidate compound, such as its binding properties, by rendering the candidate compound positioned at a unique area of the X, Y and Z-defined area of HPTPbeta. The X, Y and Z coordinates of HPTPbeta are also related to the drug candidate compound in that Applicants' inventive method involves identifying from a candidate compound those that bind or modulate the X, Y and Z-defined area of HPTPbeta as compounds useful for the treatment of an angiogenesis mediated disorder.

In sum, Applicants' claimed methods are non-obvious over "computers and various software packages listed," the Fachinger reference and any other reference at least because of the claimed inventive combination including the three-dimensional coordinates of HPTPbeta for identifying a candidate compound for the treatment of an angiogenesis mediated disorder and the functional and structural unobvious relationship between the three-dimensional coordinates of HPTPbeta and the other features required of Applicants' inventive methods. Therefore, the rejection of claims 10-32 under § 103(a) cannot properly be maintained, and Applicants respectfully request that the Examiner withdraw the rejection and pass claims 10–32 to allowance.

Conclusion

Applicants respectfully submit that the foregoing remarks demonstrate that entry of these amendments places the present application in condition for allowance, or alternatively, in better form for consideration on appeal. All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn. Applicants believe that a full and complete response has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Amendment is respectfully requested.

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to pass this application to issue.

Dated: May 21, 2007

Respectfully submitted,

By _____

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